

**REMARKS**

This is in response to the Office Action that was mailed on December 7, 2006. Claims 29-32, 37, and 41 are pending in the application.

The present invention relates to 1-(5-chloro-2-hydroxyphenyl)-5-chloro-1,3-dihydro-2H-benzimidazo-2-one and pharmaceutically-acceptable salts thereof and to their use in enhancing delivery of chemotherapeutic agents to the brain.

Claims 29-32, 37, and 41 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over EP 0 477,819 A2 and EP 0 617,023 A1. Office Action, pages 2-3. The rejection is respectfully traversed.

Applicants present herewith a 'Declaration under 37 CFR 1.132' of Dr. Morten Grunnet, which compares the compound of Example 10 in EP 0 477 819 A2 – 1-(5-chloro-2-hydroxyphenyl)-5-fluoro-1,3-dihydro-2H-benzimidazol-2-one – with the compound of present claim 29 – 1-(5-chloro-2-hydroxyphenyl)-5-chloro-1,3-dihydro-2H-benzimidazo-2-one.

These two compounds were compared to one another by Dr. Grunnet in a standard electrophysiological assay –screening on *Xenopus leavis* oocytes over-expressing human BK channels. Full details of the testing protocols used are given by Dr. Grunnet in the Rule 132 Declaration. The result of the comparative tests are presented in the Declaration. In the Declaration, the reference fluoro compound is referred to as "Compound A" and the presently claimed chloro compound is referred to as "Compound B". Testing was conducted at 10  $\mu$ M and at 30  $\mu$ M of both compounds. Based upon his analysis of the results of the testing, Dr. Grunnet

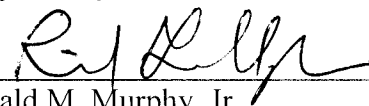
concludes that, for both concentrations, the compound of the present invention increased BK current significantly better than did the prior art compound. Dr. Grunnet indicated that this “difference was not obvious to the person skilled in the art”. The unexpected difference in properties between the presently claimed chloro compound and the prior art fluoro compound clearly rebuts any *prima facie* case of obviousness raised by structural similarity. Accordingly, withdrawal of the rejection over EP 0 477,819 A2 and EP 0 617,023 A1 is in order and is earnestly solicited.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Richard Gallagher (Reg. No. 28,781) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Dated: March 7, 2007

GMM/RG

Respectfully submitted,

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